Serum fetuin-A "a biomarker of arterial stiffness"; its relation to carotid intima media thickness in chronic kidney disease Patients

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Abstract: Objective: The aim of this study was to study the association between serum fetuin-A level as a biomarker for arterial stiffness and carotid intima media thickness (CIMT) in chronic kidney disease patients (CKD). **Background*:*** Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in CKD patients. Serum fetuin-A is a natural calcification inhibitor. Its deficiency leads to vascular calcifications and arterial stiffness. ***Methods:*** This study included forty patients with CKD, divided into 2 groups, twenty patients (12 males and 8 females) on hemodialysis therapy (H.D.) and the other twenty patients (11 males and 9 females) on conservative therapy. All the studied patients and 10 healthy control subjects were subjected to the following: through history taking and complete clinical examination, laboratory investigations: Complete Blood Count (CBC), kidney function tests (Urea & Creatinine), estimated creatinine clearance (eCCr), serum calcium & phosphorus levels, serum sodium, potassium levels, fasting blood glucose, 2 hours post prandial blood glucose, lipid profile including total cholesterol and triglycerides, liver function tests (total bilirubin, serum albumin, prothrombin time), serum fetuin-A: measured by ELISA, CIMT measured through ultrasonographic examination of carotid arteries. **Results*:*** Serum fetuin-A significantly negatively correlated with CIMT in both H.D. and conservative groups of patients with arterial stiffness, also serum fetuin-A significantly negatively correlated with serum creatinine, blood urea and positively significantly correlated with estimated glomerular filteration rate (eGFR). The mean value of serum fetuin-A is significantly reduced in the H.D. group patients compared to other two groups. The mean value of CIMT is higher in the H.D. group patients compared to other two groups. **Conclusion*:*** Serum fetuin-A is significantly reduced in CKD patients (both on conservative and H.D. therapy) with more reduction in H.D patients than in patients on conservative therapy.

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Key words: Arterial stiffness, Carotid intima media thickness, Chronic kidney disease, Cardiovascular calcification, Hemodialysis, Serum fetuin-A.

1. Introduction

Chronic kidney disease is a worldwide public health problem and is now recognized as a common condition that is associated with an increased risk of cardiovascular disease and chronic renal failure **[1].** Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients with chronic kidney disease. The spectrum of CVDs in patients with chronic kidney disease involves 3 main pathological forms: altered cardiac geometry and mechanics (left ventricular hypertrophy), accelerated atherosclerosis of both large arteries and coronaries, and arteriosclerosis. The coronary plaque in dialysis patients is a more advanced and complex lesion characterized by greater degree of medial thickness and calcification. One key element of this high CV burden appears to be arterial stiffness, as an expression of premature vascular aging **[2]**. Increased arterial stiffness in renal patients may be a consequence of chronic volume overload, vascular calcification, inflammation, endothelial dysfunction, oxidative stress and several other factors. Increased arterial stiffness has significant clinical consequences: Isolated systolic hypertension, left ventricular hypertrophy and failure, and reduced myocardial perfusion. Arterial stiffness is measured by carotid intima media thickness **[3].** Recent clinical studies have shown that lower serum fetuin A are associated with vascular calcification and cardiovascular mortality among patients with chronic kidney disease **[4].**Observational studies have shown that low serum fetuin A may be an independent risk factor for premature death in CKD patients, and patients with mildly elevated serum fetuin A levels could have a survival advantage over those with lower fetuin A levels **[5].** In this study, we tried to assess the relationship between serum fetuin-A and the risk of cardiovascular diseases (assessed by CIMT) in the patients with chronic kidney diseases. So we aimed to study serum fetuin-A as a biomarker of arterial

stiffness and correlate it to CIMT in CKD patients.

2. Patients and Methods

This study was conducted on 40 patients with chronic kidney disease attending Haemodialysis Unit and Outpatient Clinics of Medical Department of Menufia University Hospital –Egypt and 10 healthy control individuals during the period from December, 2012 to February, 2013. The study was approved by the local ethical committee of the university Hospital and a written concept was taken from all included subjects. The study population was divided into 3 groups- Group I (CKD patients on conservative therapy - Predialysis group) Included twenty CKD patients (stages 3 and 4) on conservative treatment (11males and 9 females) – Group II (CKD on regular hemodialysis therapy) Included twenty CKD patients on regular H.D, 3 sessions / week for more than 9 months (12 males and 8 females –Group III (Control group)**:** Included 10 healthy individuals (5 males and 5 females). All the studied patients and 10 healthy control subjects were subjected to the following: thorough history taking and complete clinical examination, Laboratory Investigations: - routine investigations: complete blood Count (CBC), kidney function tests (Urea & Creatinine), estimated creatinine clearance (eCCr), serum electrolytes: Serum calcium & phosphorus levels, serum sodium & potassium levels,fasting blood glucose, 2 hours post prandial blood glucose, estimation of lipid profile (including total cholesterol and triglycerides), liver function tests (total bilirubin, serum albumin, prothrombin time.) -Special investigations: Serum fetuin-A: measured by ELISA, carotid intima media thickness: measured through ultrasonographic examination of carotid arteries using a 5 to 10 MHz transducer. This was done for the right and left common carotid arteries.

- Methods of sampling:

From each subjects, under complete aseptic technique, 5ml venous blood samples were collected. Samples were allowed to clot, then were centrifuged at 1000 xg for 10 minutes within one hour after collection. A part of the separated serum is aliquoted and stored frozen at–20 c for subsequent determination of serum fetuin-A.

-Assessment of serum fetuin –A:

Principle of the assay: The kit assay Human Fetuin-A level in the sample, use purified Human Fetuin-A anti body to coat microtitre plate wells, make solid –phase antibody, then add Fetuin-A to wells, combined fetuin-A antibody which with enzyme labeled, become antibody-antigen-enzyme-antibody complex, after washing completely, Add substrate, substrate becomes blue color. At HRP enzyme-catalyzed, reaction is terminated by the addition of a sulphuric acid solution and the color change is measured spectrophotometrically at a wavelength of 450 nm. The concentration of Human Fetuin-A in the samples is then determined by comparing the O.D. of the samples to the standard curve. Manufactured by WKEA MED SUPPLIES CORP**.**

- Measurement of Carotid intima media thickness:

Measurement of intimal–medial thickness of carotid arteries through ultrasonographic examination of carotid arteries using duplex probe (11 L) of G E Divid 9 ultrasound imaging system. This was done for the right and left common carotid arteries. Longitudinal views of the layers of the normal carotid wall demonstrate two nearly parallel echogenic lines separated by a hypo echoic to anechoic region.The first echo, bordering the vessel lumen, represents the lumen–intimal interface, the second echo caused by the media–adventitia interface. The media is the anechoic/hypo echoic zone between the echogenic lines. The distance between these two lines represents the combined thickness of the intima and the media. The normal carotid intima- media thickness is up to 0.6mm **[3].**

Statistical analysis:

Data was statistically analyzed using SPSS (Statistical package for social science). Data was expressed as mean ± SD and analyzed by using student's t- test for comparison between two groups,using f-test for comparison between three groups and correlation coefficients. Differences were regarded as $P > 0.05$ non significant, $P < 0.01$ highly significant while $P < 0.05$ significant

3.Results:

The Laboratory characteristics of the studied subjects shows a significant reduction ($p<0.005$) in group I and group II patients compared to the control group (G III) as regard hemoglobin (Hb), hematocrit (Hct), eGFR, serum calcium, high density lipoprotein (HDL), alkaline phosphatase, serum albumin and serum fetuin-A levels. On the other hand, the blood levels of white blood cells (WBCs), urea, creatinine, potassium, phosphorus, total cholesterol and triglycerides are significantly increased in G I and G II patients compared to healthy controls (G III), (Table 1 and Figure 1).

The CIMT is highly significantly increased in right CCMT(Rt CCIMT) in G I (0.737 ± 0.010) and G II (0.77 ± 0.11mm) compared to control group (0.51 ± 0.06 mm); $p < 0.001$.It is also highly significantly increased in the left CCIMT (Lt CCIMT) in G I (0.73 ± 0.11 mm) and G II (0.79±0.14 mm) compared to G III(0.53±0.06 mm), $p < 0.001$.The mean CCIMT of GI (0.73±0.10 mm) and G II (0.78±0.12 mm) is highly significantly increased compared to healthy control

subjects (0.52±0.06 mm), $p < 0.001$, (Table 2 and Figure 2).

Arterial stiffness as assessed by CCIMT (≥0.6 mm) and reduction of serum fetuin- A levels ≤ 478 ng/ml is determined in all H.D. patients (100%) and in 16 patients (80%) on conservative therapy, (Tables 3, 4 and 5). In patients on conservative therapy with arterial stiffness (n = 16), the serum fetuin –A level is significantly negatively correlated with Rt CCIMT (r = -0.753), Lt CCIMT (r = - 0.756) and mean CCIMT (r = -0.759), $p < 0.001$ (Table 3 and Figure 3). In H.D. patients, the serum fetuin-A level is highly significantly negatively correlated with Rt CCIMT (r = -0.715), Lt CCIMT (r = -0.738) and mean CCIMT (r = -0.771), $p < 0.001$ (Table 4 and Figure 4). It is also significantly negatively correlated with serum calcium (r = -0.471, p <0.042), total cholesterol (r = -0.655, p = 0.002) and triglycerides (r = -0.512, p =0.025), (Table 5 and Figure 5).

Table 1: Laboratory characteristics of the studied subjects

	Group							
	Conservative(n=20)		Hemodialysis(n=20)		Control (n=10)			
	$\overline{X} \pm SD$	Range	$\overline{X} \pm SD$	Range	$\overline{X} \pm SD$	Range	F	Sig.
Hb gm/dl	10.2 ± 1.0	8.5 - 12.0	9.8 ± 1.1	7.5 -11.3	14.4 ±.5	13.7 -15.1	78.3	**< 0.001***
HCT %	33.1% ± 3.5%	27% - 33%	30.1% ± 1.5%	26.7% -38.4%	45.5% ± 5%	38.1% -51.8%	86.2	**< 0.001***
Platelets	244 ± 43.46	150 – 320	232.5 ± 57.9	150 -350	240 ± 56.96	160 – 350	0.25	> 0.05
WBCs	6.72 ± 1.27	5 - 9.2	7.95 ± 1.6	5 – 11	6.07 ± 1.12	4 - 7.8	7.24	**< 0.01***
FBS mg/dl	109 ± 37	65 – 210	106 ± 61	64 – 241	68 ± 4	63 – 77	3.02	> 0.05
2hPPBS mg/dl	158 ± 52	110 – 300	175 ± 75	110 – 330	131 ± 6	122 – 140	1.9	> 0.05
UREA mg/dl	88 ± 37	44 – 145	133 ± 38	81 – 214	32 ± 5	25 – 40	31.3	**< 0.001***
CREAT mg/dl	2.66 ± 1.03	1.5 - 4.7	9.5 ±.95	8.10 - 11.90	0.95 ± 0.13	0.70 - 1.10	424.8	**< 0.001***
eGFR ml/min	35.26 ± 14.79	17.44 - 63.3	9.71 ± 0.98	7.80 - 11.60	119.2 ± 4.78	106.9 - 123.3	436.7	**< 0.001***
Na mmol/ l	141 ± 3	135 -146	142 ± 3	135 – 146	140 ± 2	137 – 143	1.8	> 0.05
K mmol/ l	4.5 ±.5	3.8 -5.3	4.8 ±.4	4.2 - 5.4	4.1 ±.4	3.5 - 4.8	11.69	**< 0.001***
Ca mg/dl	7.4 ±.7	6 -8.4	9.1 ±.4	8.3 - 9.8	9.3 ±.5	8.5 - 10.1	58.98	**< 0.001***
P04 mg/dl	5 ±.6	4 - 6.3	5.4 ±.5	4.6 - 6.5	3.5 ±.5	2.9 - 4.1	42.6	**< 0.001***
Serum uric acid mg/dl	5.7 ± 1.8	2.8 - 8.1	6.5 ± 1.4	4.6 - 9.1	5.7 ±.7	4.1 - 6.7	1.83	>0.05
Total Cholesterol mg/dl	211 ± 24	172 – 250	230 ± 37	180 – 300	181 ± 11	163 – 200	9.5	**< 0.001***
T.G. mg/dl	148 ± 18	120 -195	154 ± 17	130 – 180	129 ± 12	112 -147	7.4	**< 0.01***
T. Bil. mg/dl	0.9 ± 0.2	.5 -1.2	0.8 ± 0.2	0.5 - 1.2	0.7 ±0.3	0.4 - 1.2	1.6	> 0.05
ALP iu/L	76 ± 21	45 – 110	106 ± 29	45 – 149	113 ± 22	79 – 145	10.6	**< 0.001***
Alb g /dl	3.8 ±.3	3.5 - 4.3	3.7 ±.4	3.0 - 4.5	4.2 ±.5	3.5 - 4.9	5.4	**< 0.01***
PT sec	19 ± 27	11 – 133	12 ± 1	11 – 14	12 ± 1	11 – 13	0.9	> 0.05
Fetuin-A ng/ml	489 ± 74	390 – 620	376 ± 50	220 -560	498 ± 58	400 – 580	10.8	**< 0.001***

* significant.

Hb: Hemoglobin, Hct: Hematocrit value, WBCs: White blood cells, FBS: Fasting blood sugar, 2hrs PPBS: 2 hours post prandial blood sugar, Creat: Creatinine, eGFR: Estimated glomerular filteration rate, Na: sodium, K: Potassium, Ca: Calcium, Po4: Phosphorus, T.G: Triglycerides, T. Bil.: Total bilirubin, ALP: Alkaline phosphatase, Alb: Albumin, PT: Prothrombin time.

Table (2): CIMT of the studied subjects

	Group						F	Sig.
	Conservative (n=20)		Hemodialysis (n=20)		Control (n=10)			
	$\overline{X} \pm SD$	Range	$\overline{X} \pm SD$	Range	$\overline{X} \pm SD$	Range		
RCCIMTmm	0.73±0.10	0.55- 0.89	0.77± 0.11	0.60 - 1.00	0.51± 0.06	0.43- 0.60	**23.6**	**<0.001***
LCCIMT mm	0.73±0.11	0.55- 0.89	0.79 ± 0.14	0.62- 1.08	0.53± 0.06	0.41- 0.60	**17.8**	**<0.001***
Mean CCIMT mm	0.73±0.10	0.57- 0.89	0.78 ± 0.12	0.62-.99	0.52± 0.06	0.43– 0.6	**21.9**	**<0.001***

* Highly significant

RCCIMT: Right common carotid intima media thickness, LCCIMT: Left common carotid intima media thickness, Mean CCIMT: Mean common carotid intima media thickness

Table (3): Correlation coeffient between serum fetuin –A and CCIMT in conservative group with and without aterial stiffness.

	Conservative group (G=I) (n=20)			
Fetuin –A / CCIMT	Without stiffness (n=4)		With stiffness (n=16)	
	r	P-value	r	P-value
RCCIMT mm	-0.721	0.488	-0.753	<0.001*
LCCIMT mm	-0.397	0.740	-0.756	<0.001*
Mean CCIMT mm	-0.945	0.212	-0.759	<0.001*

* significant

RCCIMT: Right common carotid intima media thickness, LCCIMT: Left common carotid intima media thickness, Mean CCIMT: Mean common carotid intima media thickness

Table (4): Correlations coeffient between serum fetuin –A and CIMT in haemodialysis group.

Fetuin-A / CIMT	H.D. group (G II) (no=20)	
	r	P value
RCCIMTmm	-0.715	0.001*
LCCIMTmm	-0.738	<0.001*
CCIMTmm	-0.771	<0.001*

* significant

H.D.: Hemodialysis, RCCIMT: Right common carotid intima media thickness, LCCIMT: Left common carotid intima media thickness, Mean CCIMT: Mean common carotid intima media thickness, CIMT: Carotid intima media thickness.

Table (5): Correlation coefficient between serum fetuin –A and lab. characteristics in hemodialysis group (II):

serum fetuin –A / lab. Characteristic	H.D. group (G II) (no=20)	
	r	*P* – value
Hb g/dl	0.237	0.328
HCT%	-0.213	0.382
Platelets	0.132	0.591
WBCs	-0.219	0.367
FBS mg/dl	-0.023	0.926
2hr PPBS mg/dl	-0.060	0.807
UREA mg/dl	-0.403	0.087
CREAT mg/dl	-0.378	0.111
eGFR ml/min	0.017	0.946
Na mmol/l	-0.292	0.226
K mmol/l	-0.073	0.766
Ca mg/dl	-0.471	**0.042***
P04 mg/dl	0.171	0.485
S.uric acid mg/dl	0.181	0.457
Total Cholesterol mg/dl	-0.655	**0.002***
TG mg/dl	-0.512	**0.025***
TBIL mg/dl	-0.258	0.286
ALP iu/L	0.410	0.081
ALB g/l	-0.163	0.505
PT sec	-0.166	0.497

* significant

Hb: Hemoglobin, Hct: Hematocrit value, WBCs: White blood cells, FBS: Fasting blood sugar, 2hrs PPBS: 2 hours post prandial blood sugar, Creat: Creatinine, eGFR: Estimated glomerular filteration rate, Na: sodium, K: Potassium, Ca: Calcium, Po4: Phosphorus, T.G: Triglycerides, T. Bil.: Total bilirubin, ALP: Alkaline phosphatase, Alb: Albumin, PT: Prothrombin time, H.D.: Hemodialysis.

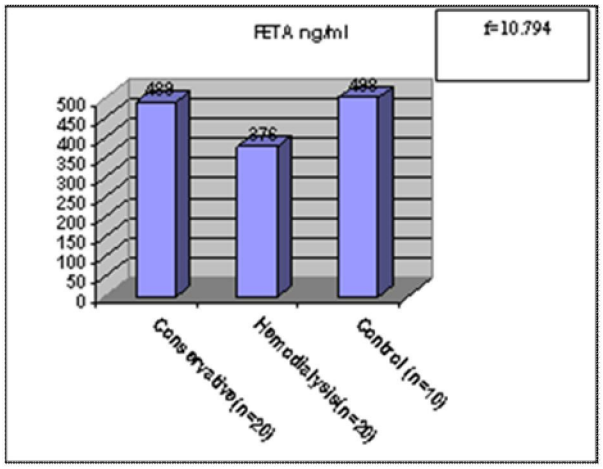

Fig.(1): Mean serum fetuin-A level (ng/ml) in the studied groups.

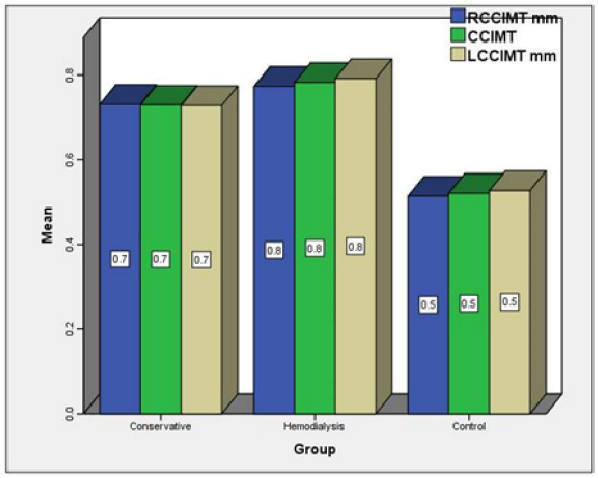

Fig.(2): R CCIMT, L CCIMT and mean CCIMT in the studied groups.

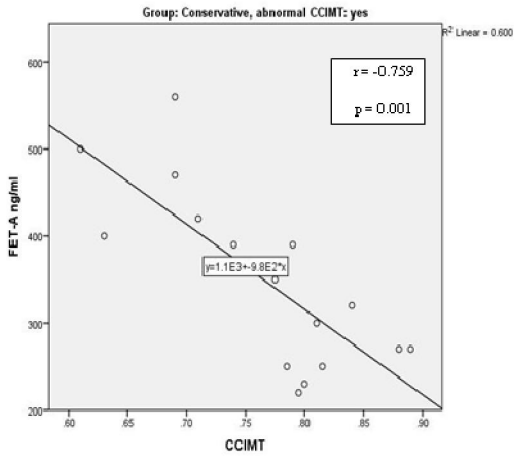

Fig.(3): correlation coeffient between s. fetuin-A and mean CCIMT in conservative group with arterial stiffness.

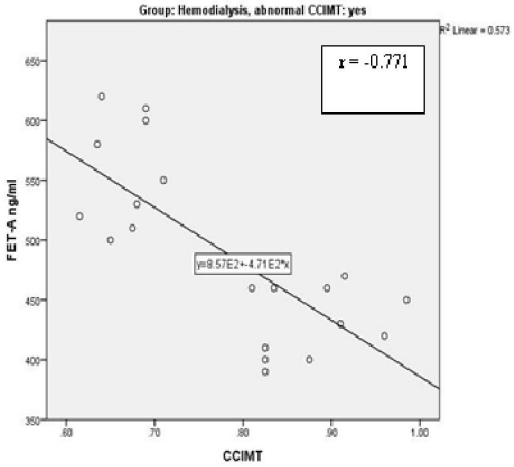

Fig.(4): correlation coeffient between s. fetuin-A and mean CCIMT in haemodialysis group with arterial stiffness.

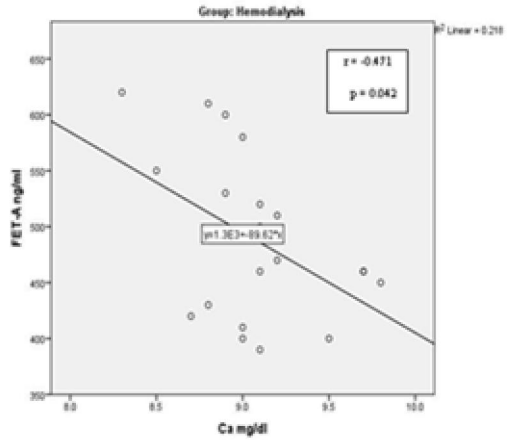

Fig.(5): Correlation coeffient between serum fetuin-A and serum ca mg/dl in haemodialysis group with arterial stiffness.

4.Discussion:

Chronic kidney disease is a worldwide public health problem and is recognized as a common condition that is associated with an increased risk of cardiovascular disease and chronic renal failure, cardiovascular disease is the leading cause of mortality and morbidity in patients with chronic kidney disease **[6].**The spectrum of CVDs in patients with chronic kidney disease involves 3 main pathological forms: altered cardiac geometry and mechanics (left ventricular hypertrophy), accelerated atherosclerosis of both large arteries and coronaries, and arteriosclerosis. The coronary plaque in dialysis patients is a more advanced and complex lesion characterized by greater degree of medial thickness and calcification. One key element of this high CV

burden appears to be arterial stiffness, as an expression of premature vascular aging. Increased arterial stiffness in renal patients may be a consequence of chronic volume overload, vascular calcification, inflammation, endothelial dysfunction, oxidative stress and several other factors. Increased arterial stiffness has significant clinical consequences: Isolated systolic hypertension, left ventricular hypertrophy and failure, and reduced myocardial perfusion. Chronic kidney disease can eventually lead to end-stage renal disease, which requires dialysis or kidney transplantation. Most people with chronic kidney disease will die of cardiovascular disease before developing kidney failure **[2].**The prevalence of CVD is increased among patients in all stages of CKD. The Cardiovascular Health Study analysis demonstrated that per every 10 mL/min per 1.73 m^2 decrease in glomerular filtration rate (GFR) the risk of CVD and all-cause mortality increased by 5% and 6%, respectively **[7].** Studies in end-stage renal disease (ESRD) populations have consistently shown that lower fetuin-A levels are associated with cardiovascular disease (CVD) events and all-cause mortality. Most but not all studies in ESRD have also reported that low fetuin-A levels are associated with coronary or abdominal aortic calcification. However, the associations of fetuin-A with subclinical CVD events in the general population are much less clear [**2].** The aim of this work is to study the relationship between the serum fetuin –A level and arterial stiffness in patients with chronic kidney disease on conservative treatment versus chronic kidney disease on regular hemodialysis therapy. In this study forty patients with CKD were divided into 2 groups: Group 1 CKD on conservative therapy and Group 2 CKD on RHD therap**y**. Results of the present study revealed that there is significant negative correlation between serum fetuin-A level & CIMT in both patients with CKD on RHD & patients with CKD on conservative treatment. Several studies similarly reported that s. fetuin-A showed a negative association with CIMT in stable chronic HD patient**s [4]. Also Wang *et al.* [5]** reported that low serum fetuin-A is associated with vascular calcification in patients on HD. **Ketteler *et al.* [8]** reported that vascular calcification is common in the study population and is associated with a lower serum fetuin-A level. High or sustained-normal serum fetuin-A levels may have a protective role against the development of vascular calcification in HD patients. **Ix *et al.* [9]** demonstrated an inverse association between serum fetuin-A and carotid intima-media thickness in HD patients. It has also been shown that *in vitro* fetuin-A is a potent inhibitor of the calcification process and that experimental fetuin-A deficiency appears to promote vascular calcification **[4].** Several non-mutually exclusive theories or mechanisms have been advanced to explain the onset and progression of vascular calcification, during which a central role is played by the vascular smooth muscle cells (VSMCs) that compose the medial layer of the vessel wall. Initially, a soluble amorphous calcium– phosphate complex is deposited in presence of excessive calcium phosphate mineral. It is unlikely to cause harm if stabilized effectively by inhibitory proteins, such as fetuin A, carboxylated matrix Gla protein (MGP) and osteopontin, and by the inorganic inhibitory compound pyrophosphate [**10].**The pathogenesis of vascular calcification is not well understood, but it is likely to be multifactorial. Abnormalities in mineral metabolism, particularly hyperphosphataemia as well as the loss of circulating and/or local mineralization inhibitors such as fetuin A, matrix Gla protein (MGP), initially lead to the formation and deposition of Ca/P nanocrystals. Furthermore, Ca/P nanocrystals as well as inorganic phosphate (Pi) induce the expression of genes that promote the calcification/mineralization process such as bone morphogenetic protein 2 (BMP2) and bone GLA protein(BGP), while at the same time repressing the expression of fetuin-A, MGP, factors that are known to inhibit the progression of calcification. This causes a transdifferentiation of VSMCs to osteoblast-like cells, ultimately resulting in vessel calcification. fetuin-A is a potent inhibitor of spontaneous hydroxyapatite formation from supersaturated calcium- and phosphate-containing solutions **[10].** Fetuin-A stabilizes colloidal nanoscopic complexes with Ca and P and prevents crystal growth by shielding mechanisms, the complex formed is termed "calciprotein particles" because they share functional and structural similarities to lipoprotein particles like low-density lipoproteins. Fetuin-A is responsible for about 50% of the precipitation- inhibitory effect in serum and extracellular fluids **[9].** The mean values of K^+, Ca, PO_4 are significantly high in the studied HD patients. Hyperkalemia is a common problem in dialysis patients **[6]**, in a study reported by **Checheriţă *et al.* [11]** showed that native vitamin D deficiency and secondary hyperparathyroidism are noted early in the course of CKD. Treatment for secondary hyperparathyroidism is often accompanied by several side effects esp. Cardiovascular. Hypercalcaemia and increased calcium phosphorus product with vascular and coronary calcification have been documented after excessive calcium containing phosphate binders and/or vitamin D therapy **[11].** The mean values of T.cholesterol and T.G. are significantly higher in the studied H.D. patients than in the conservative patients. In a study reported by **Chan *et al.* [12]** showed that the prevalence of

hyperlipidemia or dyslipidemia is much higher in HD patients compared to the general population. Total or low density lipoprotein LDL cholesterol is highest in patients with chronic renal impairement. The mean value of serum fetuin A is significantly lower in the HD group with mean ±SD (376±50 ng/ml) than in the conservative group with mean ±SD (489±74 ng/ml). In a study reported by **Ketteler *et al. [8]*** performed in 312 HD patients, investigating serum fetuin A levels in relations to outcomes, serum fetuin A levels were lower in patients on hemodialysis when compared to control populations. This may be due to exposure to high levels of uremic toxins down regulating hepatic fetuin A production, in addition, calcification could consume fetuin A from the circulation. The present study showed that the mean value of CIMT was significantly higher in the hemodialysis group than in the conservative group. In a study reported by **Dursun *et al. [13]*** there was a significant increase in CIMT in the uremic and HD groups compared to healthy controls. The HD group had the highest CIMT values indicating a higher risk for atherosclerosis in HD patients using carotid ultrasonography. **Takamura *et al. [14]*** determined that serum creatinine is independent determinants of CIMT, **Ossareh S, et al *[15]*** *found that* CIMT was greater in HD patients compared to control groups. The mean value of serum fetuin A was lower in the studied HD patients with arterial stiffness than in conservative group with arterial stiffness and it was significantly negatively correlated with CIMT. As serum fetuin A is a calcification inhibitor its deficiency predispose to arterial stiffness in HD patients because uremia suppress fetuin -A level ***[4].*** A study by **Moe *et al. [4]*** determined that fetuin A levels inversely correlate with the calcification and atherosclerosis burdens**. Stenvinkel *et al.* [16]** concluded that fetuin A deficiency seems to be a key element of the malnutrition inflammation atherosclerosis syndrome.

In conclusion: Serum fetuin-A level was significantly reduced in CKD patients (both HD and conservative patients) with much significant reduction in H.D patients than in conservatively treated patients. It is also significantly negatively correlated with CIMT in both groups of studied patients. Thus, reduction of serum fetuin-A level can be a risk factor for the occurrence of CVD in CKD patients.

5/23/2014

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